## REMARKS

Claims 1-29 are pending in the application. Claims 1-4 and 8-24 were withdrawn from consideration, leaving claims 5-7 and 25-29 subject to examination. Claims 5-7 and 25-29 were objected to due as being in improper dependent form for failing to further limit the subject matter of a previous claim; claims 5-7 and 25-29 were rejected under 35 U.S.C. § 112, second paragraph; claim 27 was rejected under 35 U.S.C. § 112, first paragraph (enablement); claims 5-7, 28, and 29 were rejected under 35 U.S.C. § 112, first paragraph (written description); and claims 5-7 and 25-29 were rejected under 35 U.S.C. § 102(b). The objection and each of the rejections are addressed as follows.

First, Applicants note that, as was helpfully suggested by the Examiner, an Application Data Sheet is submitted herewith to correct the address of inventor Juan Arroyo.

Applicants also note that the claims have been amended to specify chimeric flaviviruses including one particular mutation: a reversion at position 279 of an attenuated Japanese encephalitis virus. In addition, the claims now specify vaccine compositions. Applicants respectfully request that the latter amendment not be considered as resulting in a change in restriction group, as non-elected Group I included claims to both viruses (claims 1-4 and 10-13) and vaccine compositions including such viruses (claim 14). Thus, permitting the present claims (originally drawn to viruses, similar to claims 1-4 and 10-13 of Group I) to be amended to specify vaccine compositions is consistent with the restriction requirement.

Applicants finally submit, for the Examiner's reference, papers showing protective efficacy of a chimeric virus including a yellow fever virus capsid and non-structural proteins and Japanese encephalitis virus pre-membrane and envelope proteins (Guirakhoo et al., Virology

257(2):363-372, 1999; Monath et al., J. Virol. 74(4):1742-1751, 2000).

Claim Objection

Claims 5-7 and 25-29 were objected to as being in improper dependent form for failing to further limit the submit matter of a previous claim. This objection has been met by the present amendments to the claims, by which each of the dependent claims now further limits the scope of the subject matter of a previous claim. Applicants thus request that this objection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 5-7 and 25-29 were rejected under 35 U.S.C. § 112, second paragraph for indefiniteness. The Examiner first states that the chimeric flavivirus of claim 5 includes a Japanese encephalitis virus envelope protein with a hinge region mutation, and that the mutation is present in a region of a yellow fever virus envelope protein. The Examiner further questions the meaning of the term "corresponding to" in this claim. In response, Applicants note that the present claims have been amended to specify that the mutation is in a particular amino acid of the Japanese encephalitis virus envelope protein, and the claim no longer includes the term "corresponding." Applicants thus request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph (enablement)

Claim 27 was rejected under 35 U.S.C. § 112, first paragraph for lack of enablement, on the basis that this claim specifies Japanese encephalitis virus strain SA14-14-2, and that the specification does not provide a repeatable method for obtaining this strain. Based on this, the

Examiner requires that the strain be deposited.

Applicants respectfully request reconsideration of this rejection, as the sequence of Japanese encephalitis virus strain SA14-14-2 was well known in the art at the time of Applicants' filing date. Based on this information, those of skill in the art could readily make the chimeras of the present claims, without undue experimentation. This sequence information is provided, for example, in Nitayaphan et al., Virology 177:541-552, 1990; Aihara et al., Virus Genes 5(2):95-109, 1991; Ni et al., J. Gen. Virol. 75:1505-1510, 1994; and Ni et al., J. Gen. Virol. 76:409-413, 1995 (copies are enclosed).

The current case law and the M.P.E.P. supports Applicants' submission that a deposit should not be required. In particular, in *Falko-Gunter Falkner v. Inglis* (Fed. Cir. 2006, 05-1324), the Federal Circuit affirmed a Board decision that a claim specifying a vaccine composition comprising a mutant poxvirus having an inactivating mutation in an essential gene was enabled, without providing corresponding sequence information. On this matter, the Court stated

> With respect to a skilled artisan's abililty to identify "essential" poxvirus genes, as discussed below we note that there was undisputed testimony that as of the time of filing of the earliest Inglis application publications in professional journals had disclosed the DNA sequence of the poxvirus genome along with the locations of the 'essential regions.' The person of ordinary skill in the art would clearly have possessed such knowledge, and given the ready accessibility of the journals, the absence of incorporation by reference is not problematic. Indeed, '[a] patent need not teach, and preferably omits, what is well known in the art.' *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987).

Applicants further note that M.P.E.P. 2404.02 provides:

> Applicant may show that a deposit is not necessary even though specific biological materials are required to practice the invention if those biological materials can be made or isolated without undue experimentation. Deposits may

be required to support the claims if an isolation procedure requires undue experimentation to obtain the desired biological material. *Ex Parte Jackson*, 217 USPQ 804 (Bd. App. 1982). No deposit is required, however, where the required biological materials can be obtained from publicly available material with only routine experimentation and a reliable screening test. *Tabuchi v. Nubel*, 559 F.2d 1183, 194 USPQ 521 (CCPA 1977); *Ex Parte Hata*, 6 USPQ2d 1652 (Bd. Pat. App. & Int. 1987).

In view of the above, Applicants request that this rejection be withdrawn.

The above notwithstanding, Applicants further submit that a strain including SA14-14-2 pre-membrane and envelope sequences and yellow fever virus capsid and non-structural proteins was deposited on behalf of the present Applicants under the terms of the Budapest Treaty with the American Type Culture Collection (see page 8 of the application; ATCC VR-2594; also see the enclosed deposit receipt and supporting documentation).

Rejection under 35 U.S.C. § 112, first paragraph (written description)

Claims 5-7, 28, and 29 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the embodiments that are adequately described are chimeras having the E279 reversion of Japanese encephalitis virus and the substitutions of lysine position 202 or 204 of Dengue virus. As is noted above, the claims now specify a mutation that has been deemed by the Examiner to be adequately described: the E279 reversion. In view of this amendment, Applicants request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 5-7 were rejected under 35 U.S.C. § 102(b) as being anticipated by Chambers et

al., J. Virology 73(4):3095-3101, 1999. In maintaining this rejection, the Examiner states "Chambers discloses that the JEV envelope region has a mutation (i.e., reversion) at position 279 in the hinge region (see Tables 3-4). This mutation is expected to result in decreased viscerotropism of the chimeric virus."

Applicants first note that the present claims specify a reversion, which means a change from the attenuated mutation in SA14-14-2 (E279M) to the wild-type sequence (E279K). In the cited Tables, Chambers describes viruses including the wild-type sequence of Japanese encephalitis envelope protein (YF/JE-N, JE-N, and JE SA-14) and viruses including the attenuated sequence of JESA-14-14-2 (JE-SA-14-14-2 and YF/JE-S). Table 4 shows amino acid differences between these viruses. Chambers does not describe a virus in which the attenuated sequence includes a single reversion to wild-type, at position 279, as is required by the present claims. Rather, in the instances in which Chambers describes the wild-type sequence at position 279, it is in the context of other wild-type sequences in the envelope protein (see Table 3). Thus, as Chambers does not describe the presently claimed virus, Applicants respectfully request that this rejection be withdrawn.

Claims 5-7 were also rejected under 35 U.S.C. § 102(b) as being anticipated by Arroyo et al., J. Virology 75(2):934-942, 2001. The Examiner states that Arroyo discloses a yellow fever virus/Japanese encephalitis virus chimera that includes a lysine at position 279 of the hinge region. In response, we note that the current claims specify vaccine compositions (see claim 5, above). The focus of the study of Arroyo is the characterization of the contribution of amino acids differing between vaccine (SA 14-14-2) and wild-type (Nakayama) strains of Japanese encephalitis virus to neurovirulence. In the Arroyo study, the amino acids are reverted

individually and in combination (see, e.g., Table 3) to assess the impact of reversions on neurovirulence. Arroyo does not suggest use of the revertants, such as the E279 revertant, in vaccine compositions. Arroyo therefore does not anticipate the present claims.

Applicants further note that Arroyo does not render the present claims obvious, as Arroyo teaches that reversion of E279 increases neurovirulence (see, e.g., Table 3, and page 939, last paragraph of the left column: "...reversion at $E_{279}$ appeared to increase neurovirulence..."). Thus, based on this reference, there would not have been motivation to use the E279 revertant in the form of a vaccine composition. However, the experiments described in the present application show that the E279 revertant has unexpectedly beneficial properties with respect to viscerotropism, which in turn render it to be a vaccine candidate (see, e.g., pages 12-23). Thus, Applicants submit that an obviousness rejection of claims specifying the E279 revertant in the context of a vaccine composition should not be made over the Arroyo reference.

Provisional Obviousness-Type Double Patenting Rejection

Claims 5 and 6 were provisionally rejected under the judicially-created Doctrine of Obviousness-Type Double Patenting over claims 1, 2, and 4 of co-pending application no. 10/345,036. When the only rejection remaining in a case is a provisional double patenting rejection, an application should be allowed to issue. M.P.E.P. § 822.01. In view of the amendments and remarks provided herein, Applicants submit that all of the grounds of rejection in this case, other than the double patenting rejection, have been met. Accordingly, the double patenting rejection should be withdrawn and the case allowed to issue.

## CONCLUSION

Applicants submit that the claims are in condition for allowance and such action is respectfully requested. Although no charges are believed to be due, if there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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